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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/922,958	08/07/2001	Lorenz Poellinger	3743/49008	9818

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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/922,958	POELLINGER ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33 and 35-66* is/are pending in the application.

4a) Of the above claim(s) *1-32, 37-39 amd 43-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33, 35-36 and 40-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to the Amendment

The Amendment filed on 12/28/2005 in response to the previous Non-Final Office Action (9/21/2005) is acknowledged and has been entered.

Claims 1-33 and 35-66 are currently pending

Claims 1-32, 37-39 and 43-66 are withdrawn from consideration as being drawn to non-elected inventions.

Claims 33, 35-36 and 40-42 are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejections Maintained:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33 and 35-36 **remain** rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As set forth previously, "an isolated protein according to claim 29" is the isolated polypeptide of Claim 1 comprising an amino acid sequence of SEQ ID NO: 4 and fragments thereof with an altered PYI motif at residues 564-566. In the instant case, claims 33-36 are inclusive of a genus of molecules identified as comprising an amino acid sequence set forth in SEQ ID NO: 4 or any fragments and/or mutants thereof that bind to a genus of target proteins and fragments thereof referred to as "VHL". While claims 40-42 are inclusive of a genus of molecules referred to as having a "PYI motif" or functional fragments thereof and a genus of molecules referred to as

"P564 spanning protein" or functional fragments thereof. However, the written description only sets forth two fragments of SEQ ID NO: 4 (SEQ ID NOs: 5 and 6), each of which comprise a PYI motif or p564 spanning protein, used together with VHL (SEQ ID NO: 2) for methods of identifying agents.

The specification teaches (page 9, paragraph 0026-0027) that methods for identifying agents of the present invention includes, but is not limited to, polypeptides having at least an amino acid of SEQ ID NO: 5 (minimum N-TAD) or a smaller fragment thereof, SEQ ID NO: 6 (residues 547-575), or described mutants thereof and the VHL protein (SEQ ID NO: 2). With regards to the mutants, the specification teaches (Pages 6-7) that the mutants comprise altered amino acid residues such as; an altered PYI motif at residues 564-566, a ^{564}P, a $^{565\text{-}566}$YI, ^{565}Y, a $^{569\text{-}571}$DDD, ... ect.. The specification further teaches (page 13, paragraph 0042) that additional methods for identifying agents of the invention include, but are not limited to, polypeptides comprising a PYI motif or p564 spanning polypeptide (residues 547-575) or portion thereof. Thus, it appears that a p564 spanning polypeptide consists of the same amino acids as disclosed for SEQ ID NO: 6. However, the written description only sets forth two fragments of SEQ ID NO: 4 (SEQ ID NOs: 5 and 6), each of which comprise a PYI motif or p564 spanning protein, used together with VHL (SEQ ID NO: 2) for identifying agents. Therefore, the written description does not commensurate with the full scope of any fragments and/or variants of SEQ ID NO: 4 or any fragments of the VHL protein (SEQ ID NO: 2).

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification

provides neither a representative number of molecules that bind VHL nor does it provide a description of structural features that are common to SEQ ID NO: 4. Further, the specification fails to provide a representative number of molecules referred to as VHL along with a description of structural features that are common to the VHL. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of all the fragments of SEQ ID NO: 4 and VHL, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a VHL protein (SEQ ID NO: 2) and two fragments of SEQ ID NO: 4,(SEQ ID NOs: 5 and 6), which comprise the PYI motif and p564 spanning protein, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

In response to the rejection, Applicants contend that the claims have been amended which are believed to obviate this rejection.

The amendments and argument have been carefully considered, but are not found persuasive.

With regards to the amendment, the Examiner acknowledges that SEQ I DNO: 2 has been inserted into the currently pending claims. However, the written description only sets forth the amino acid sequence of SEQ ID NO: 2 in combination with binding to the amino acid of SEQ ID NO: 4; and therefore is not commensurate with the full scope of any fragments of SEQ ID NO: 2 which interact with the amino acid sequence of SEQ ID NO: 4.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 40-42 remain rejected under 35 U.S.C. 102(b) as being anticipated by Maxwell et al. (Nature 1999; 399: 271-275, IDS).

Maxwell discloses a method of evaluating an antagonist of the PYI motif for VHL-HIF-1 alpha interacting inhibiting efficacy; comprising: determining a reference level of VHL-HIF-1 alpha interacting in a cell or group of cells; administering said antagonist to an equivalent test cell; measuring the level of VHL-HIF-1 alpha interaction in said test cell; and determining said antagonist is efficacious when the measured test level of VHL-HIF-1 alpha interaction is less than the reference level of VHL-HIF-1 alpha interaction (page 273, 1st column, 1st full paragraph to 2nd column). The reference further teaches that the test were done at both normoxic and hypoxic conditions (page 273, 1st column, 1st full paragraph to 2nd column). Thus, while the Maxwell et al. does not specifically state that the inhibitor is an agonist of the PYI motif, the claimed functional limitation would be an inherent property of the referenced method because as evidenced by Tanimoto et al. (EMBO 2000; 19: 4298-4309, IDS), the highly conserved core motif, i.e. PYI, of the N-TAD of HIF-1 alpha is critical for interaction with VHL (specifically page 4303, 1st column, 1st full paragraph). Thus, it does not appear that the claim language or limitation results in a manipulative difference in the method

steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

In response to this rejection, Applicants contend that while Maxwell et al. discloses a method of evaluating a PYI antagonist, Maxwell fails to disclose the method set forth in the amended claims which relies on SEQ ID NO:s 4, 5 and 6, wherein the sequence comprises the critical PYI motif.

This argument has been carefully considered, but is not found persuasive.

In response to Applicants argument that Maxwell fails to disclose the method set forth in the amended claims which relies on SEQ ID NO:s 4, 5 and 6, the Examiner recognizes that Maxwell et al. does not specifically teach the method requiring the amino acids consisting of SEQ ID NO: 4 or 5 or the oligonucleotide of SEQ ID NO: 6. However, the claims as currently amended do not appear to be solely drawn to SEQ ID NO:'s 4, 5 and 6. For example, the claims recite a method of evaluating an antagonist of the PYI motif **or** a protein encoded by one of SEQ ID NO:s 4,5 or 6 (emphasis added). Thus, as stated *supra* and admitted by Applicants, Maxwell teaches a method of evaluating a PYI antagonist.

New Objections:

Specification

The disclosure is objected to because of the following informalities: Page 1, line 4 recites "incline numberinglinecluding" which appears to be a typo.

Appropriate correction is required.

New Rejections necessitated by Amendment:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 40-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In the instant case, claim 40 is drawn to a method of evaluating an antagonist of the PYI motif or a protein encoded by one of SEQ ID NO:s 4, 5, or 6. However, the sequence represented as SEQ ID NO: 4 and 5 are amino acid sequences and not a nucleic acid sequence which encodes a protein. Thus, it is unclear what applicants are attempting to claim.

Claim 40 recites the limitation "said target protein" in claim 40. However, after careful review of the pending claims there does not appear to be a recitation of a target protein. As such, there is insufficient antecedent basis for this limitation in the claim. It is suggested that the limitation "target protein" be amended to recite the SEQ ID NO: 2.

All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.

Therefore, NO claim is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
3/1/06